

CLAIMS AMENDMENTS

Please cancel claims 32 and 33 without prejudice.

Please amend the claims as follows:

Claims 1-28 (cancelled)

29. (currently amended) An isolated oligonucleotide hybridizable under stringent conditions, corresponding to 40% formamide with 5x or 6x SSC, to the nucleic acid molecule encoding on expression a soluble leptin receptor polypeptide selected from the group consisting of:

- a. a DNA molecule of SEQ ID NO:1, 3, 5, 7, or 9;
- b. a DNA molecule complementary to the DNA molecule defined in (a);
- c. a DNA molecule which is amplifiable ~~identifiable~~ with a polymerase chain reaction (PCR) probe selected from group consisting of a probe for clone 7 (forward primer SEQ ID NO:42 and reverse primer SEQ ID NO:43), a probe for clone 11 (forward primer SEQ ID NO:44 and reverse primer SEQ ID NO:45), and both clone 7 and clone 11; and
- d. a DNA molecule that codes on expression for the soluble leptin receptor polypeptide encoded by any of the foregoing DNA molecules.

30. (currently amended) An isolated oligonucleotide hybridizable under stringent conditions, corresponding to 40% formamide with 5x or 6x SSC, to the nucleic acid molecule which codes on expression for a soluble leptin receptor polypeptide selected from the group consisting of:

a. a soluble leptin receptor selected from the group consisting of ~~OB-Ra (SEQ ID NO:2), OB-Rb (SEQ ID NO:4), OB-Re (SEQ ID NO:6), OB-Rd (SEQ ID NO:8), and OB-Re (SEQ ID NO:10)~~, or allelic variants thereof; and

b. a leptin receptor comprising amino acids 28-805 of SEQ ID NO:10, ~~selected from the group consisting of:~~

i. ~~— N terminal corresponding to OB-Ra through Lys⁸⁸⁹ and C terminal corresponding to a C terminal selected from the group consisting of OB-Rb after Lys⁸⁸⁹ (SEQ ID NO:86), OB-Re after Lys⁸⁸⁹ (SEQ ID NO:87), and OB-Rd after Lys⁸⁸⁹ (SEQ ID NO:88);~~

ii. ~~— N terminal corresponding to OB-Rb or OB-Re through Lys⁸⁸⁹, and C terminal corresponding to OB-Ra after Lys⁸⁸⁹ (SEQ ID NO:89,90) or OB-Rd after Lys⁸⁸⁹ (SEQ ID NO:91,92);~~

iii. ~~— N terminal corresponding to OB-Rd through Lys⁸⁸⁹, and C terminal~~

corresponding to OB-Ra after Lys⁸⁸⁹ (SEQ ID NO:93), OB-Rb after Lys⁸⁸⁹ (SEQ ID NO:94), or OB-Re after Lys⁸⁸⁹ (SEQ ID NO:95);

iv. N terminal corresponding to SEQ ID NO:84 from Pro⁶⁶⁴ to Lys⁸⁸⁹, and C terminal corresponding to OB-Ra after Lys⁸⁸⁹ (SEQ ID NO:96), OB-Rb after Lys⁸⁸⁹ (SEQ ID NO:97), OB-Re after Lys⁸⁸⁹ (SEQ ID NO:98), or OB-Rd after Lys⁸⁸⁹ (SEQ ID NO:99);

v. N terminal corresponding to SEQ ID NO:84 from Met⁷³³ to Lys⁸⁸⁹, and C terminal corresponding to OB-Ra after Lys⁸⁸⁹ (SEQ ID NO:100), OB-Rb after Lys⁸⁸⁹ (SEQ ID NO:101), OB-Re after Lys⁸⁸⁹ (SEQ ID NO:102), or OB-Rd after Lys⁸⁸⁹ (SEQ ID NO:103);

vi. N terminal selected from the group consisting of OB-Ra, OB-Rb, OB-Rd, and SEQ ID NO:84 from Pro⁶⁶⁴ through His⁷⁹⁶, and OB-Re from His⁷⁹⁶ (SEQ ID NO:104,105,106 and 107); and

vii. N terminal corresponding to SEQ ID NO:84 from Met⁷³³ to His⁷⁹⁶, and OB-Re from His⁷⁹⁶ (SEQ ID NO:108);

c. a leptin receptor wherein

- i. the N terminal sequence is selected from the group consisting of
- (1) amino acid residues 1-889 (SEQ ID NO:109);
 - (2) amino acid residues 23-889 (SEQ ID NO:110);
 - (3) amino acid residues 28-889 (SEQ ID NO:111);
 - (4) amino acid residues 133-889 (SEQ ID NO:112);
 - (5) amino acid residues 733-889 (SEQ ID NO:113);
 - (6) amino acid residues 1-796 (SEQ ID NO:114);
 - (7) amino acid residues 23-796 (SEQ ID NO:115);
 - (8) amino acid residues 28-796 (SEQ ID NO:116);
 - (9) amino acid residues 28-796 preceded by an N-terminal Asp-Pro dipeptide (SEQ ID NO:117);
 - (10) amino acid residues 133-796 (SEQ ID NO:118); and
 - (11) amino acid residues 733-796 (SEQ ID NO:119); and

ii. the C terminal sequence is selected from the group consisting of

- (1) SEQ ID NO:11;
- (2) SEQ ID NO:12;
- (3) SEQ ID NO:13;
- (4) SEQ ID NO:14; and
- (5) SEQ ID NO:15 after His⁷⁹⁶ (SEQ ID NO:120);

d. a leptin receptor having an amino acid sequence selected from the group consisting of

~~i. Asp Arg Trp Gly Ser Tyr⁴²⁰ (SEQ ID NO:77) → Pro⁶⁴¹ (SEQ ID NO:121,122);~~

~~ii. Asp Arg Trp Gly Ser Ser⁴¹⁸ (SEQ ID NO:78) → Pro⁶⁴¹ (SEQ ID NO:123,124);~~

~~iii. Asp Arg Trp Gly Ser Leu⁴²³ (SEQ ID NO:79) → Val³³¹ (SEQ ID NO:125,126); and~~

~~e. a leptin receptor as described in (a) (d) above in which a cysteine is substituted with an amino acid selected from the group consisting of serine, threonine, and alanine;~~

~~wherein the numbering is based on the amino acid sequence of SEQ ID :84.~~

31. (currently amended) An isolated oligonucleotide hybridizable under stringent conditions, corresponding to 40% formamide with 5x or 6x SSC, to the nucleic acid molecule having a nucleotide sequence corresponding or complementary to the DNA sequence set forth in SEQ ID NO:1, 3, 5, 7 ~~or~~ 9.

Claims 32- 66 (cancelled)

67. (withdrawn and currently amended) A method for diagnosing body weight abnormalities in a mammal comprising detecting splice variants of soluble leptin receptor OB-R in a patient sample comprising contacting a sample suspected of containing splice variants of soluble leptin receptor OB-R with an oligonucleotide hybridizable under stringent conditions, corresponding to 40% formamide with 5x or 6x SSC, to the nucleic acid molecule which codes on expression for a soluble leptin receptor polypeptide selected from the group consisting of:

a. a leptin receptor selected from the group consisting of OB-Ra, OB-Rb, OB-Rc, OB-Rd, and OB-Re (SEQ ID NO:10), or allelic variants thereof; and

b. a leptin receptor comprising amino acids 28-805 of SEQ ID NO:10. selected from the group consisting of:

- i. N terminal corresponding to OB-Ra through Lys⁸⁸⁹ and C terminal corresponding to a C terminal selected from the group consisting of OB-Rb, OB-Rc, and OB-Rd after Lys⁸⁸⁹;
- ii. N terminal corresponding to OB-Rb or OB-Rc through Lys⁸⁸⁹, and C terminal corresponding to OB-Ra or OB-Rd after Lys⁸⁸⁹;
- iii. N terminal corresponding to OB-Rd through Lys⁸⁸⁹, and C terminal corresponding to OB-Ra, OB-Rb, or OB-Rc after Lys⁸⁸⁹;
- iv. N terminal corresponding to SEQ ID NO:55 from Pro⁶⁶⁴ to Lys⁸⁸⁹, and C terminal corresponding to OB-Ra, OB-Rb, OB-Rc, or OB-Rd after Lys⁸⁸⁹;
- v. N terminal corresponding to SEQ ID NO:55 from Met⁷³³ to Lys⁸⁸⁹, and C terminal corresponding to OB-Ra, OB-Rb, OB-Rc, or OB-Rd after Lys⁸⁸⁹;
- vi. N terminal selected from the group consisting of OB-Ra, OB-Rb, OB-Rd, and SEQ ID NO:55 from Pro⁶⁶⁴ through His⁷⁹⁶, and OB-Re from His⁷⁹⁶; and
- vii. N terminal corresponding to SEQ ID NO:55 from Met⁷³³ to His⁷⁹⁶, and OB-Re from His⁷⁹⁶; and

b. a leptin receptor wherein

i. the N terminal sequence is selected from the group consisting of

- (1) amino acid residues 1-889;
- (2) amino acid residues 23-889;
- (3) amino acid residues 28-889;
- (4) amino acid residues 133-889;
- (5) amino acid residues 733-889;
- (6) amino acid residues 1-796;
- (7) amino acid residues 23-796;
- (8) amino acid residues 28-796;
- (9) amino acid residues 28-796 preceded by an N terminal Asp-Pro dipeptide;
- (10) amino acid residues 133-796; and
- (11) amino acid residues 733-796; and

ii. the C terminal sequence is selected from the group consisting of

- (1) SEQ ID NO:11;
- (2) SEQ ID NO:12;
- (3) SEQ ID NO:13;
- (4) SEQ ID NO:14; and
- (5) SEQ ID NO:15 after His⁷⁹⁶;

c. a leptin receptor having an amino acid sequence selected from the group consisting of

- i. Asp-Arg-Trp-Gly-Ser-Tyr⁴²⁰ (SEQ ID NO:77) → Pro⁶⁴¹;
- ii. Asp-Arg-Trp-Gly-Ser-Ser¹¹⁸ (SEQ ID NO:78) → Pro⁶⁴¹;
- iii. Asp-Arg-Trp-Gly-Ser-Leu¹²³ (SEQ ID NO:79) → Val³³⁴; and

d. a leptin receptor as described in (a)-(d) above in which a cysteine is substituted with an amino acid selected from the group consisting of serine, threonine, and alanine; wherein the numbering is based on the amino acid sequence of SEQ ID NO:55.

68. (withdrawn and currently amended) A method for diagnosing body weight abnormalities in a mammal comprising detecting splice variants of soluble leptin receptor OB-R in a patient sample comprising contacting a sample suspected of containing splice variants of soluble leptin receptor OB-R with an oligonucleotide hybridizable under stringent conditions, corresponding to 40% formamide with 5x or 6x SSC, to the nucleic acid molecule which codes on expression for a polypeptide selected from the group consisting of SEQ ID NOS: ~~2, 4, 6, 8 and 10~~, or allelic variants thereof.

69. (withdrawn and currently amended) A method for measuring the expression of splice variants of soluble leptin receptor OB-R in a patient sample comprising contacting a sample suspected of containing splice variants of soluble leptin receptor OB-R with an oligonucleotide hybridizable under stringent conditions, corresponding to 40% formamide with 5x or 6x SSC, to the nucleic acid molecule which codes on expression for a polypeptide selected from the group consisting of:

- a. a leptin receptor selected from the group consisting of ~~OB-Ra, OB-Rb, OB-Re, OB-Rd, and OB-Re (SEQ ID NO:10)~~, or allelic variants thereof; and
- b. a leptin receptor comprising amino acids 28-805 of SEQ ID NO:10, selected from the group consisting of:

- i. ~~N terminal corresponding to OB-Ra through Lys⁸⁸⁹ and C terminal corresponding to a C-terminal selected from the group consisting of OB-Rb, OB-Re, and OB-Rd after Lys⁸⁸⁹;~~
- ii. ~~N terminal corresponding to OB-Rb or OB-Re through Lys⁸⁸⁹, and C terminal corresponding to OB-Ra or OB-Rd after Lys⁸⁸⁹;~~
- iii. ~~N terminal corresponding to OB-Rd through Lys⁸⁸⁹, and C terminal corresponding to OB-Ra, OB-Rb, or OB-Re after Lys⁸⁸⁹;~~
- iv. ~~N terminal corresponding to SEQ ID NO: 55 from Pro⁶⁶⁴ to Lys⁸⁸⁹, and C terminal corresponding to OB-Ra, OB-Rb, OB-Re, or OB-Rd after Lys⁸⁸⁹;~~
- v. ~~N terminal corresponding to SEQ ID NO:55 from Met⁷³³ to Lys⁸⁸⁹, and C terminal corresponding to OB-Ra, OB-Rb, OB-Re, or OB-Rd after Lys⁸⁸⁹;~~
- vi. ~~N terminal selected from the group consisting of OB-Ra, OB-Rb, OB-Rd, and SEQ ID NO:55 from Pro⁶⁶⁴ through His⁷⁹⁶, and OB-Re from His⁷⁹⁶; and N terminal corresponding to SEQ ID NO:55 from Met⁷³³ to His⁷⁹⁶, and OB-Re from His⁷⁹⁶; and~~

e. ~~a leptin receptor wherein~~

- i. ~~the N terminal sequence is selected from the group consisting of~~

- (1) ~~amino acid residues 1-889;~~
- (2) ~~amino acid residues 23-889;~~
- (3) ~~amino acid residues 28-889;~~
- (4) ~~amino acid residues 133-889;~~
- (5) ~~amino acid residues 733-889;~~
- (6) ~~amino acid residues 1-796;~~
- (7) ~~amino acid residues 23-796;~~
- (8) ~~amino acid residues 28-796;~~
- (9) ~~amino acid residues 28-796 preceded by an N-terminal Asp-Pro dipeptide;~~
- (10) ~~amino acid residues 133-796; and~~
- (11) ~~amino acid residues 733-796; and~~

- ii. ~~the C terminal sequence is selected from the group consisting of~~
- (1) ~~SEQ ID NO:11;~~
 - (2) ~~SEQ ID NO:12;~~
 - (3) ~~SEQ ID NO:13;~~
 - (4) ~~SEQ ID NO:14; and~~
 - (5) ~~SEQ ID NO:15 after His⁷⁹⁶;~~
- d. ~~a leptin receptor having an amino acid sequence selected from the group consisting of~~
- i. ~~Asp Arg Trp Gly Ser Tyr⁴²⁰ (SEQ ID NO:77) → Pro⁶⁴¹;~~
 - ii. ~~Asp Arg Trp Gly Ser Ser¹⁴⁸ (SEQ ID NO:78) → Pro⁶⁴¹;~~
 - iii. ~~Asp Arg Trp Gly Ser Leu¹²³ (SEQ ID NO:79) → Val³³¹; and~~
- e. ~~a leptin receptor as described in (a) (d) above in which a cysteine is substituted with an amino acid selected from the group consisting of serine, threonine, and alanine;~~
- wherein the numbering is based on the amino acid sequence of SEQ ID NO:55.

70. (withdrawn and currently amended) A method for measuring the expression of splice variants of soluble leptin receptor OB-R in a patient sample comprising contacting a sample suspected of containing splice variants of soluble leptin receptor OB-R with a oligonucleotide hybridizable under stringent conditions, corresponding to 40% formamide with 5x or 6x SSC, to the nucleic acid molecule which codes on expression for a polypeptide selected from the group consisting of SEQ ID NOS: 2, 4, 6, 8 and 10, or allelic variants thereof.

71. (withdrawn) The method of any of claims 67-70 wherein the oligonucleotide is labeled.

72. (withdrawn) The method of any of claims 67-70 wherein the nucleic acid molecule is RNA.

73. (withdrawn and currently amended) The method of any of claims 67-70 wherein the oligonucleotide is selected from the group consisting of SEQ ID NO: 20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, ~~SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54.~~